UNITED STATES DISTRICT COURT
FOR THE
DISTRICT OF MASSACHUSETTS

JOHN HANCOCK LIFE INSURANCE COMPANY, JOHN HANCOCK VARIABLE LIFE INSURANCE COMPANY, and MANULIFE INSURANCE COMPANY (f/k/a INVESTORS PARTNER LIFE INSURANCE COMPANY),	CIVIL ACTION NO. 05-11150-DPW
Plaintiffs,	
v.	
ABBOTT LABORATORIES,	
Defendant.	

JOHN HANCOCK'S RESPONSE TO ABBOTT'S OBJECTIONS TO THE AFFIDAVIT OF WILLIAM R. FAIRWEATHER, PH.D

Plaintiffs John Hancock Life Insurance Company, John Hancock Variable Life Insurance Company and Manulife Insurance Company (collectively, "John Hancock" or "Hancock") hereby respond to Abbott Laboratories' ("Abbott") objections to the Affidavit of William R. Fairweather, Ph.D (the "Fairweather Affidavit").

Abbott makes two baseless objections to the Fairweather Affidavit. First, it asserts that Dr. Fairweather is offering opinions not disclosed in his expert report. Dr. Fairweather's report disclosed his primary opinion: on March 12, 2001, Abbott's statisticians should have known that the M99-114 clinical trial for ABT-594 would likely be a failed study because it failed to reach its enrollment target, suffered a high premature termination rate, and because its subjects suffered a high rate of adverse events for nausea, vomiting and dizziness. (Report at 12, attached

to Abbott's Motion as Ex. A.) Moreover, Abbott went ahead on May 31, 2007 and deposed Dr. Fairweather. In response to Abbott's questions, Dr. Fairweather elaborated on the *precise* opinions Abbott now claims he never disclosed; namely, the impact of imputed data in clinical studies and the reaction of the FDA to the M99-114 trial. Second, Abbott incorrectly claims that Dr. Fairweather is opining regarding Abbott's state of mind. On the contrary, he is simply stating, based on more than thirty years experience as a statistician, what a reasonable statistician at a major pharmaceutical company knew or should have known regarding the viability of the M99-114 trial based on the facts available to Abbott. Abbott's objections to his affidavit should be overruled.

Discussion

I. BECAUSE ABBOTT HAD FULL NOTICE OF THE OPINIONS CONTAINED IN THE FAIRWEATHER AFFIDAVIT, THOSE OPINIONS ARE TIMELY UNDER THE RULES.

Rule 26(a)(2)(B) requires that an expert report contain "a complete statement of all opinions the witness will express and the basis and reasons for them." Where a party has not complied with Rule 26(a)(2)(B), the testimony should be admitted if the non-disclosure was justified or harmless. *See* Fed. R. Civ. P. 37(c)(1). Significantly, Rules 26(a)(2)(B) and 37(c)(1) "are not designed to prohibit a witness from testifying about anything not explicitly mentioned in [the expert's] Rule 26 disclosure, but rather to protect one party from being blindsided by another party with new opinions never before discussed." *Cary Oil Co., Inc. v. MG Refining & Marketing, Inc.*, 2003 WL 1878246 at *4 (S.D.N.Y. April 11, 2003); *see also Muldrow ex rel. Estate of Muldrow v. Re-Direct, Inc.*, 493 F.3d 160, 167 (D.C. Cir. 2007).

Indeed, Rule 26(a)(2)(B) "does not limit an expert's testimony simply to reading his report … The rule contemplates that the expert will supplement, elaborate upon, [and] explain...

his report in his [trial] testimony." *Muldrow*, 493 F.3d at 167. Moreover, issues explored at an expert's deposition put a party on notice that those issues are among the opinions that the expert might testify to at trial. *See, e.g.*, *Smith v. Tenet Healthsystem SL, Inc.*, 436 F.3d 879 (8th Cir. 2006) (while expert witness did not include reliance on x-rays in his pretrial disclosure, discussion of x-rays during deposition put plaintiff on notice and rendered Rule 26 violation harmless); *Baldauf v. Davidson*, 2007 WL 2155967 at *8 (S.D. Ind. July 24, 2007).

A. Dr. Fairweather's Expert Report Placed Abbott On Notice Regarding The Opinions Set Forth In His Affidavit.

Abbott claims that the Fairweather Affidavit (*i.e.*, ¶¶ 25, 29, 41, 42, and 43) states "new opinions that were not disclosed" in his initial expert report. Abbott is attempting to do just what the case law forbids: requiring that an expert report conform precisely with the expert's trial testimony. Dr. Fairweather's report indisputably put Abbott on notice of all the opinions expressed in his trial testimony.

The central opinion expressed in Dr. Fairweather's report is that: "[b]y March 12, 2001, I believe that Abbott's statistical staff were, or should have been, aware that the M99-114 study would be substantially underpowered to reach its objective." (Report at 12). In support of his opinion, Dr. Fairweather explicitly noted that Abbott prematurely terminated enrollment in the study, and that enrolled subjects suffered a high rate of premature terminations for nausea, vomiting and dizziness. (*Id.* at 12-13).

Abbott contends that the Fairweather Affidavit uses a different "usable sample" of subjects than the report. (Motion at 1). This is not correct. Dr. Fairweather opined in his report, and he testifies now, that "actual power would depend on the distribution of these patients among the dose groups [premature terminators and competers], but it would fall between these two values." (Report at 12). Abbott curiously complains that Dr. Fairweather never opined in his

report regarding "the alleged reactions of the FDA to the use of such data." (Motion at 1). In fact, he expressed that very opinion: "From my experience at the FDA, and my review of the documents as of March 12, 2001, it is my opinion that the statisticians at a reasonable pharmaceutical company, such as Abbott Laboratories, would realize that ABT-594 would face serious questions that might, at the very least, delay or prevent its entry into Phase III." (Report at 13).

Although it fails to actually identify any "new opinions," Abbott feigns surprise at the Fairweather Affidavit's use of the clinical protocol for M99-114. His report is replete with references to the protocol. For example, Dr. Fairweather states he "was asked to assess the available statistical analyses and related reports regarding Abbott Laboratories' clinical trial known as M99-114." (Report at 3).

Moreover, Dr. Fairweather indisputably put Abbott on notice that he would further elaborate on and support the opinions in his report based on documents or deposition testimony that he would review prior to trial. (*Id.* at 9). That is exactly what he did. In many cases, Dr. Fairweather is simply identifying Abbott's *own* documents that support his previously expressed opinions. (*See, e.g.,* Fairweather Affidavit ¶ 29 (identifying Abbott documents relating to the M99-114 clinical trial protocol); and ¶ 41 (identifying Abbott documents supporting opinion that Abbott's use of the "intent-to-treat" analysis for subjects who prematurely terminated from the M99-114 study was less reliable than other methods)).

Thus, Abbott's contention that Dr. Fairweather's trial affidavit provided new opinions is without merit.

B. Abbott Also Learned About The Opinions In Question During Its Deposition Of Dr. Fairweather.

Abbott's counsel examined Dr. Fairweather on each of his purportedly "new opinions" during his deposition on May 31, 2007. In response to the question by Abbott's counsel "can you go through the each of the opinions that you plan to offer than are contained in your report," Dr. Fairweather gave the following answer:

> Well, as of the date that this contract was signed, the 12th of March 2001, in my opinion, the statisticians at Abbott would know that the study was not going to achieve its enrollment targets and that it would be underpowered.
>
> In this case they would know that it would be substantially underpowered because there were substantial lack of reaching the target.
>
> Moreover, there was a lot of people having adverse events in this study, so that they would know that adjustments would have to be made for the sample-size calculations when the study was analyzed.
>
> When you impute data for a subject in order to do the intent to treat analysis, you can't consider a subject who has imputed data to be the same kind of data as somebody who completes the trial.
>
> And so the power would be reduced from two things, from the lack of enrollment and from the deficit in people actually completing it who start the trial.
>
> The result of that is that getting a P value that is statistically significant at the end of the study for the response variable of primary interest was going to be very difficult. Getting a significant one was going to be difficult.
>
> And that would mean – This is what we call in the trade a failed study. It doesn't mean that there's no information coming out of the study. What it means is you technically have not met the requirements for a statistically significant result.
>
> Given that there are adverse events occurring to the patients, I'm sure that the medical people reviewing a study of this kind would have concerns about the benefit/risk evaluation, are the patients getting enough benefit to justify the risks of adverse events that they would be taking.

> So it would look pretty dim for this. The possibility of going to phase III, as was the hope, I don't see how they would do that.

(Fairweather Trans. at 41-43, attached hereto as Ex. 1).

Moreover, Abbott explored Dr. Fairweather's opinions on the "imputed data and usable sample size under the procedure and methodology set forth in the clinical protocol [for ABT-594]." (Abbott's Motion at 3).

> Q: So then in your opinion, the usable sample size for the M99-114 study was 137 patients; is that correct?
>
> A: I think I would like to modify that … [T]here are only 137 patients who gave complete data. The balance up to – I think it was 250 some-odd that finished the study … were giving partial data. So those patients would also have been usable in the sense of entering into the calculation.

(Fairweather Trans. at 75; *see also* id. at 42-44, 82 85, and 100). Dr. Fairweather also testified regarding the FDA's view on the reliability of imputed data. (*Id.* at 46).

Thus, pursuant to Fed. R. Civ. P. 37(c), none of Dr. Fairweather's opinions should be precluded because Abbott had ample notice of them. As noted above, under Fed. R. Civ. P. 37(c), a "harmless" violation of Rule 26 does not mandate exclusion of the evidence. *Muldrow ex rel. Estate of Muldrow*, 493, F.3d at 167.

II. DR. FAIRWEATHER'S OPINIONS REGARDING THE FACTS OF THIS CASE ARE ADMISSIBLE UNDER FED. R. EVID. 702.

Abbott wrongly contends that Dr. Fairweather is testifying to Abbott's state of mind. (Abbott's Motion at 4). Expert testimony is admissible where: (1) the testimony is based upon sufficient facts or data; (2) the testimony is the product of reliable principles and methods; and (3) the witness has applied the principles and methods reliably to the facts of the case. Fed. R. Evid. 702. Dr. Fairweather has been offered as an expert in the field of statistical aspects of clinical trials conducted by large pharmaceutical companies such as Abbott.

Abbott's objections to the so-called "state of mind" opinions should be overruled. First, Dr. Fairweather is testifying to the conclusions that a reasonable statistician at a major pharmaceutical company should have drawn regarding the M99-114 trial as of March 12, 2001. The First Circuit has allowed the admissibility of such testimony in a factual setting remarkably similar to this one -- the significance of clinical trial results for drug compounds. *See, Maruho Company, Ltd. v. Miles, Inc.*, 13 F.3d 6, 10 (1st Cir. 1993) (Breyer, J.). (stating that plaintiff may have reached a favorable result had he presented expert testimony on what a reasonable pharmaceutical executive would have thought of an important negative drug study showing adverse events for a sublicensed compound).

Second, Abbott's claim that Dr. Fairweather is testifying about the FDA's "state of mind" is no more warranted. Dr. Fairweather has testified that the "FDA would have had serious questions about any statistical conclusions drawn from...imputed [data]." (Fairweather Affidavit, ¶ 42). Dr. Fairweather spent twenty-five years with the FDA as an "Expert Regulatory Statistician". (Fairweather Affidavit, ¶¶ 9-10). In that capacity, he considered the value of imputed data while examining "statistical...claims made by sponsors of literally hundreds of clinical trials." (*Id.* at ¶ 9). His opinion is the product of reliable principles and constitutes permissible expert testimony. *See In re Prempro Products Liability Litigation*, 2006 WL 5217764 at *6 fn. 59 (E.D. Ark. Sept 13, 2006) ("What FDA officials would have done with certain...information such as ...adverse event reports" is admissible if presented by a qualified expert).

Conclusion

For the foregoing reasons, John Hancock respectfully requests that the Court overrule Abbott's objections to the Fairweather Affidavit.

Respectfully submitted,

JOHN HANCOCK LIFE INSURANCE COMPANY, JOHN HANCOCK VARIABLE LIFE INSURANCE COMPANY and MANULIFE INSURANCE COMPANY
By their attorneys,

/s/ *Brian A. Davis*
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Date: March 3, 2008

CERTIFICATE OF SERVICE

I hereby certify that this document filed through the ECF system will be sent electronically to the registered participants as identified on the Notice of Electronic Filing (NEF), and that paper copies will be sent to those non-registered participants (if any) on March 3, 2008.

/s/ Richard C. Abati
Richard C. Abati

EXHIBIT 1

VOLUME: II

EXHIBITS: See Index

UNITED STATES DISTRICT COURT

DISTRICT OF MASSACHUSETTS

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JOHN HANCOCK LIFE INSURANCE COMPANY,
JOHN HANCOCK VARIABLE LIFE INSURANCE
COMPANY, and MANULIFE INSURANCE COMPANY
(f/k/a/ INVESTORS PARTNER INSURANCE COMPANY)

Plaintiffs Civil Action

v. No. 05-11150-DPW

ABBOTT LABORATORIES

Defendant

- x

VIDEOTAPED DEPOSITION of

WILLIAM R. FAIRWEATHER, PH.D.

Thursday, May 31, 2007

8:05 a.m.

Donnelly, Conroy & Gelhaar, LLP

One Beacon Street

Boston, Massachusetts

Michelle Keegan, Court Reporter

APPEARANCES:

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Also Present:
Maura Cunningham, Videographer

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EXHIBITS

* Original exhibits returned to Ms. Guzelsu *

PROCEEDINGS

THE VIDEOGRAPHER: Here begins videotape number 1 in the deposition of Dr. William Fairweather, Ph.D., in the matter of Hancock, et al. versus Abbott Laboratories, in the United States District Court for the District of Massachusetts, case number civil action 05-11150-DPW.

Today's date is May 31st, 2007. The time on the video monitor is 8:05. The video operator today is Maura Cunningham, contracted by Merrill Legal Solutions, 101 Arch Street, Boston, Massachusetts 02110.

This video deposition is taking place at One Beacon Street, Boston, Massachusetts and was noticed by Ozge Guzelsu of Munger, Tolles & Olson.

Counsel, please voice-identify yourselves and state whom you represent.

MR. ZWICKER: Joseph Zwicker, Choate Hall & Stewart, Boston, Massachusetts, for the plaintiffs and the witness.

MS. GUZELSU: Ozge Guzelsu, Munger, Tolles & Olson, for the defendant Abbott Laboratories.

THE VIDEOGRAPHER: The court reporter

today is Michelle Keegan of Merrill Legal Solutions.

Would the reporter please swear in the witness.

WILLIAM R. FAIRWEATHER, PH.D.
having been satisfactorily identified and duly sworn by the Notary Public, was examined and testified as follows:

DIRECT EXAMINATION

BY MS. GUZELSU:

Q. Good morning, Dr. Fairweather.
A. Good morning.
Q. Could you please state your name for the record.
A. My full name is William Ross Fairweather.
Q. And what is your current business address?
A. 15405 Narcissus Way in Rockville, Maryland.
Q. And that's also your home address?
A. That is.
Q. Have you been deposed before?
A. By?
Q. Have you been deposed before?
A. No.
Q. This is your first deposition?
A. Yes.

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Reese was observing, I think.
Q. Tom Reese was in the room. Okay. So you said you've spent 25 hours on the case since you completed your report and about four hours of it was for deposition prep. What were you doing the other --
A. Traveling up --
MR. ZWICKER: Objection. You can answer.
THE WITNESS: Sorry.
Q. What were you doing the other 20 hours?
A. Traveling up here. I think I read a couple of other depositions, one by Bruce Rhodda and one by I think it's Michael Thomas, Mr. Thomas.
Q. You probably read the expert report of Bruce Rhodda; is that correct?
A. That's quite possible.
Q. And the deposition of James Thomas?
A. James Thomas. Okay.
Q. Let's turn back to your report. On page 3, under "Task," it says, "I was asked to assess the available statistical analyses and related reports regarding Abbott Laboratories' clinical trial known as M99-114.

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"I have attempted to determine what a reasonable statistician at a pharmaceutical company such as Abbott Laboratories would know about the status and likely outcome of M99-114 as of 12 March 2001, the day before the agreement was concluded between John Hancock and Abbott Laboratories." Have I read that correctly?
A. Right.
Q. Is that the sole issue that you were asked to address when you were retained in this matter?
A. Yes. Well, that's the crux of the case, what were the representations that Abbott made to John Hancock before -- up to this date.
Q. The representations that were made to John Hancock?
A. I guess as to what the potential for profit would be and investing in this set of products that Abbott was developing.
Q. I see. And what are the representations regarding M99-114?
A. I suppose, in general terms, that this product was going to be a successful product and they were going to develop it.
Q. I understand the product, but with regard to

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the clinical trial, what were the -- Are you aware of any representations that were made by Abbott Laboratories to John Hancock regarding the clinical trial M99-114?
A. I'm thinking that I can't really answer that question other than in general terms. This is a phase II trial. It's intended to show certain scientific results leading to a phase III trial.
I don't have -- I don't recall seeing anything where something specifically was said about that trial to John Hancock.
My understanding was that John Hancock is not technically in a position to evaluate that sort of thing, that they relied on Abbott's doing the best it could kind of statement to promote their products.
Q. You are aware that John Hancock hired a scientific consultant to aid it in due diligence?
A. I'm not -- I don't remember hearing anything about that, if they did or didn't.
Q. Okay. Were you asked to render any opinions for this case that you did not feel comfortable giving?
A. Not at all.

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Q. Can you describe to me how this report was prepared.
MR. ZWICKER: Objection.
Q. You can answer.
A. How the report was prepared?
Q. What did you do from beginning to end to put this report together?
A. Okay. What led up to the report. Well, I read through an awful lot of documents, many of which were not terribly relevant to the issue as I stated it here. I thought about what should be the issue and rephrased some things to get it into this form so that I would have something concrete to go after. And at that point I started focusing on documents that would shed light on this particular question. In other words, narrowed down this mass of documents to something that was a little more tractable.
And it became obvious that power and sample-size calculations were the issue. And so I thought that it would be useful to have a general statistical statement of what's involved with doing that because to somebody who is not a statistician it's a bit arcane.

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already testified to? Because I don't think you've captured everything he testified to about what he reviewed since.

A. I think I would say no.

Q. Let's step back. Since you've -- Since you completed your report in January of this year, what additional information have you received regarding this case?

A. Other than the documents I've already talked about, I can't recall anything.

Q. And the documents we've already talked about is the expert report of Bruce Rhodda and the deposition of Jim Thomas?

A. Right. Yesterday I was given another copy of the original -- I think the word is complaint, the legal document that was filed, I guess to refresh my memory, but that was the only thing.

MR. ZWICKER: Let's go off the record for a second.

THE VIDEOGRAPHER: Going off the record. The time is 8:50.

(Recess taken)

(Record read)

THE VIDEOGRAPHER: Back on the record.

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The time is 8:52.

A. I'd like to correct my answer. When I said that I had reviewed the deposition of Jim Thomas, I included all the exhibits as meaning I had reviewed them as well, but they actually were sent to me as a separate stack of documents. Counsel reminds me that is a separate item.

Also, he had sent me a -- testimony or a deposition of Dr. McCarthy, which I think was a piece of his total deposition.

Q. So you reviewed an excerpt of the deposition of Dr. McCarthy?

A. Yes.

Q. Subsequent to preparing your report?

A. No. Subsequent to, yes.

Q. And you don't -- You probably don't --

A. Let's see. I guess that's what that list of documents you showed me --

MR. ZWICKER: Don't guess, Bill. You can talk about what you reviewed.

A. That's what I reviewed. If this is the list of the --

MR. ZWICKER: Don't speculate. The question is what you reviewed.

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A. I reviewed the excerpt -- the exhibits of Jim Thomas's deposition, whatever that list is.

Q. Full stop?

A. Full stop.

Q. And has anything that you've reviewed since you prepared your report changed the opinions that you've expressed in that report?

A. No. I might like to --

MR. ZWICKER: You've answered. It was a yes or no question. You said no. Now she gets to ask another question.

Q. You have no intention of changing any of the conclusions that are contained in your report?

A. That's correct.

Q. Are you planning on submitting a revised report?

A. I'm hesitating because I don't know what the procedure is for this.

Q. It's not a trick question. If you have current plans to submit a revised report --

A. I do not have current plans to submit a revised report.

Q. That's good enough. Your report states that it's subject to modification based on your review of

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any additional documents or other information. And as you've testified, the additional documents so far that you reviewed haven't modified any of your opinions, that's correct?

A. That's correct.

Q. Are you planning on reviewing any other documents in addition to the ones that you reviewed up until today?

A. I'm not planning on it. I'm not planning on it.

Q. All right. Does your report contain all of the opinions that you expect to testify to at trial -- testify regarding to at trial? Strike the first one.

A. Yes. I might restate some of them in better terms or something, clarifications, but basically not changing anything else.

Q. Okay. Briefly, can you go through each of the opinions that you plan to offer that are contained in your report.

MR. ZWICKER: Objection. Overbroad.

Q. You can answer.

A. Well, as of the date that this contract was signed, the 12th of March 2001, in my opinion, the

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statisticians at Abbott would know that the study was not going to achieve its enrollment targets and that it would be underpowered.

In this case they would know that it would be substantially underpowered because there were substantial lack of reaching the target.

Moreover, there was a lot of people having adverse events in this study, so that they would know that adjustments would have to be made for the sample-size calculations when the study was analyzed.

When you impute data for a subject in order to do the intent to treat analysis, you can't consider a subject who has imputed data to be the same kind of data as somebody who completes the trial.

And so the power would be reduced from two things, from the lack of enrollment and from the deficit in people actually completing it who start the trial.

The result of that is that getting a P value that is statistically significant at the end of the study for the response variable of primary interest was going to be very difficult. Getting a

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significant one was going to be difficult.

And that would mean -- This is what we call in the trade a failed study. It doesn't mean that there's no information coming out of the study. What it means is you technically have not met the requirements for a statistically significant result.

Given that there are adverse events occurring to the patients, I'm sure that the medical people reviewing a study of this kind would have concerns about the benefit/risk evaluation, are the patients getting enough benefit to justify the risks of adverse events that they would be taking.

So it would look pretty dim for this. The possibility of going to phase III, as was the hope, I don't see how they would do that.

You can't have a failed study -- I mean, on the basis of a successful study, you are allowed to go to phase III where you start broadening the patient population, putting larger numbers on the study, trying to get some definitive results for subsequent labeling of the product.

And if that requires a successful phase II to do that, logically how do you do that with an unsuccessful study? It doesn't make any sense. In

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fact, it doesn't happen. So they should have known that going to phase III was just not going to work for the study.

Based on what I reviewed, the company was clearly looking for alternative methods of delivering the product that could maybe circumvent the adverse events that were occurring and possibly carrying it forward at that point.

So it was clear that they were monitoring, in other words. So one would think that statisticians would be explaining to them the consequences if they needed numerical explanations of just how bad it was going to be. So I think they would know that as of that date.

Let's see what else I see in here.

(Pause)

A. I did mention that -- something about another -- If there were any other phase II studies that would have supported this, I didn't notice it in the documents, so I'm not aware of any that was ongoing.

So basically, if going to phase III depended on this study, I would have to conclude that that's not a likely event.

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Q. Have you reviewed -- You said you reviewed Dr. Rhodda's rebuttal report?

A. Yes.

Q. Did your review of that change any of your conclusions or analyses that you reached in your report?

A. No. His report did not focus on the key issue, as far as I could see, which is what -- I hate to say it this way, but a what did they know and when did they know it kind of approach.

I only went up to this date in March, the 12th or 13th, of 2001, because the study was still blinded at this point, so nobody had the ability to analyze the data, knowing which patients were on which treatments.

And he did some analyses in there, I think, talking about analysis of the study and reaching conclusions on the basis of unblinded data.

Q. Okay. You didn't look at any data subsequent to March 12th, 2001 for the study?

A. I can't say I didn't look at it, but it was irrelevant to the task that I stated, which is what was the status as of that date.

Q. So you don't have any opinions regarding

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whether the --
A. No.
MR. ZWICKER: Let her finish the question.
A. Sorry.
Q. That's okay. You don't have any opinions regarding whether the study reached the statistically significant endpoint?
A. No, I don't.
Q. And you weren't asked to opine on that?
A. No. The one -- Okay.
MR. ZWICKER: Do you want to amend your answer? Go ahead.
A. I was not asked to opine on it, but I did note in reviewing the documents that I don't believe this project was submitted to the FDA, so they did not get the FDA reviewer's comments back.
If I were an FDA reviewer, I would never have allowed imputed data to be treated without an adjustment as it was in the reports that I saw of the analyses. They do not appear to have made any adjustment for the fact that there was so much imputed data. This bothered me, but that was not my task, so I did not deal with it.

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Q. Okay. Let's turn to page 3 of your report, which I don't have numbered but --
MR. ZWICKER: Of Exhibit 1.
Q. Under "General Statistical Concepts" you have about six and a half pages regarding general statistical concepts.
A. Okay.
Q. Did you write this off the top of your head?
A. Yes.
MR. ZWICKER: Objection.
A. Yes.
Q. You don't refer to any reference materials in creating this section?
A. It wasn't necessary. This is standard statistical practice and theory. Every statistician knows this. In fact, it was in Bruce Rhodda's report in somewhat of a different form, but he's essentially saying the same thing.
Q. At the bottom of page 8 of your report it says, "In designing a study, it is desirable to maximize the power to the extent possible to ensure that the study has a very good chance of rejecting the null hypothesis, i.e. of demonstrating there is an advantage to the test product." What did you

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mean by "the extent possible"?
A. Well, when you do that, the way you do it is to refine your method of measurement to the best of your ability, because that cuts down the variation, and to increase the sample size to the extent that you can because that -- if you take the ratio variance over N, that makes that variable get smaller, which is what you want.
The thing is that companies will run into economic restrictions on how many subjects they're willing to put into the study. So that's what I meant by "to the extent possible." To the extent that a company is willing to fund it. That may be a factor of time as well. If it takes a long time to recruit patients, that would be a limitation.
Q. On the top of page 9 of your report it says, "One way to decrease," and I believe that's sigma squared, "is to measure the study outcome as precisely as possible." What did you mean by that statement?
A. Well, in some cases a sponsor will try to use a rating scale of a certain kind to make their measurements. That's going to be the basis of the

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study, so I've administered this rating scale to the patients.
If that's a highly variable instrument, it's maybe not the best one that they could use. If they were to spend some time developing a better scale, they might get less variation, a more reproducible result out of each patient. That would help cut down the variation.
Q. And is variation the same thing as standard deviation? Are they sort of referred to as interchangeable terms?
MR. ZWICKER: Objection. You can answer.
A. They're not interchangeable terms. Technically, variation is the square of the standard deviation. Used colloquially, I guess it would be -- "variation" just means what the common English word means for "variation."
If you tried to measure the same thing over and over and over again in a biological material, you don't get the same answer because there is variation.
Q. And you're stating that it's important to have this variation measured as precisely as

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is not foreign -- These considerations are not foreign to me.

Q. Were you retained in this matter as a statistical expert, Dr. Fairweather?

A. Technically, I'm not sure about that. I was retained, I believe, as an expert witness. I'm not sure that the -- that a specialty is part of that designation.

Q. An expert witness regarding clinical trials generally, pharmaceutical companies?

MR. ZWICKER: Objection. You can answer.

A. I think it was as an expert witness in this matter. I'm just barely remembering that, but I think that's the case.

Q. Okay. Could you turn to page 12 of Exhibit 1, which is your report. The first sentence on the top of page 12, "The tracking of enrollment and premature terminations around this time," and then there's a citation, "would have indicated that the usable sample size would be only 137 patients (269 enrolled less 132 terminated), not the 320 planned"; is that correct? That's what it says here.

A. Yes.

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Q. So then in your opinion, the usable sample size for the M99-114 study was 137 patients; is that correct?

MR. ZWICKER: Objection.

A. I think I would like to modify that. That probably should have been more elaborated to say that the -- there are only 137 patients who gave complete data.

The balance up to the -- I think it was 250 some-odd that finished the study, which probably wasn't known at that time, were giving partial data. So those patients would also have been usable in the sense of entering into the calculation.

How usable would depend on just how much data they were able to provide. Obviously, if they stayed in the study until the end, except for one day, most of their data is there. If they left the study after the first day, most of this data is missing.

So the 137 would be a lower limit, if you will, of usable data. I shouldn't have been so succinct with that statement.

Q. So if a patient enrolled in a study and stayed in the study for two weeks, they would provide some data regarding the efficacy of ABT-594; is that correct?

MR. ZWICKER: Objection.

A. I'm not remembering exactly the schedule for collecting data, but if data were collected in those two weeks, yes.

Q. Okay. Any data -- If any data was collected, it would be --

A. We're talking about the primary efficacy response variable here.

Q. So the fact that certain patients dropped out of the study didn't necessarily mean that they were not usable in terms of calculating the results from the M99-114 study?

MR. ZWICKER: Objection.

A. It didn't necessarily mean that, but I didn't have access to exactly when the patients dropped, how much data was available on each one and so on. And besides, that was something after the date that we're talking about in 2001.

Q. Sometime after that -- I see. So the fact that there were only 137 usual patients was just as of the date of March 12th, 2001?

A. No, I don't believe that's correct. I

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believe that they knew what their enrollment was as of that date. If I'm not mistaken -- I'm not supposed to speculate on that.

As of that date they knew that there were more patients who had entered the study than that, so there was some partial amount of data on these other patients. I'm just not aware of how much partial data there was.

Q. But that partial data would have been used in Abbott's analysis of the M99-114 study; is that correct?

A. Yes.

MR. ZWICKER: Objection.

A. It would be used but not without adjustment.

Q. When would that adjustment occur? After the results had been unblinded?

A. Yes. Could I modify that response? It could be used if anybody needed to recalculate the power.

In other words, if you start a power calculation saying -- simple case, saying, How many patients do we need if everybody completes the study? That's a very simple calculation. In this case the answer would be 320.

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on a particular patient; is that correct?
MR. ZWICKER: Objection. You can answer.
A. Yes, I believe I stated that.
Q. Okay. And in this -- In your report on page 12, in the middle paragraph it says, "If, in the more likely scenario, the 137 available patients had been distributed evenly across the dose groups, with approximately 34 in each group, the power would have been less than 50 percent," and then there's a citation. That's what your report states; is that correct?
A. Correct.
Q. But if there were more than 137 patients with available data, i.e. patients who had terminated but still had some data available, that would change the power of the study at that point, would it not?
A. Yes.
MR. ZWICKER: Objection.
Q. So if there were 150 patients and 13 of them, for example, had terminated halfway through the study but there was still data to be collected, then you would use that data as well, and that would

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change this power calculation?
MR. ZWICKER: Objection.
A. This was intended to be a worst case scenario, showing the range of possible powers that would have been contemplated as of the date that I looked at the -- In other words, this is saying -- I'm trying to put myself in the position of people looking at the information that was available at the time and saying how good could it be, how bad could it be.
How bad it could be might be that only 137 patients are giving data that is usable. What does that do? What would the power have been if that were the case for the effect size and variation that we thought at the beginning of this study? And that's the calculation.
And that was taken, I believe, from close to their own calculations. I believe I did not do those.
Q. Although the results of the M99-114 study were double-blinded, would Abbott have had information on whether it had actually collected data from the patients who had dropped out before the end of the study? Just on whether it had

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actually collected data. Not on what the data was, but whether there was a collection of data for any study that had terminated, patient that had terminated early on.
A. I don't know that they -- what information they would have on something like that because of the process of -- in a clinical trial of putting the data together. Different companies do it in different ways.
So I'm not sure what Abbott would have available to it in terms of how much of the data on the patients who dropped out, how much would be available.
Q. So let's assume for a second that Abbott was for each patient that had terminated also keeping track of how many data points they had collected for each of those patients. Under that scenario, would Abbott then be able to estimate how many of the patients that had terminated would have useful data?
MR. ZWICKER: Objection.
Q. Terminated before the -- preterminated before the end of the study.
A. Yes, I would think so.

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Q. And in that case, then, they would be able to say, Although these 50 patients preterminated, they went two, three weeks throughout the study. We can use their data. And that would affect our power calculation as follows?
MR. ZWICKER: Objection.
A. I believe that that's correct.
Q. Okay. So when you say here the 137 available patients, that is a worst case scenario assumption?
A. Yes.
Q. That none of the terminated patients had any available data that could be used for the calculations at the end of the study?
MR. ZWICKER: Objection. Go ahead.
Q. Is that correct?
A. Yes.
Q. But that's not necessarily the case. If Abbott had been collecting data points for those terminated patients and knew how many of those patients had data, that number would likely be greater than 137?
MR. ZWICKER: Objection.
A. Yes, that's correct.

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Q. Is there anywhere in this document that discusses the M99-114 study and the dropout rate?

MR. ZWICKER: What document are we talking about, for the record? Exhibit 7?

MS. GUZELSU: Exhibit 7.

A. I'm not sure that they mention which study they're basing this on, but from the timing of the document I would think that it is that study that is causing them to discuss this. They're talking about the tolerability of that.

Q. Wasn't there an earlier study with --

MR. ZWICKER: Are you done with your answer, by the way?

THE WITNESS: Yes, I am.

Q. I'm sorry. Wasn't there an earlier study with completed data that they could also be discussing, the osteoarthritis study that you discussed on page 10 of your report?

MR. ZWICKER: Objection. Calls for speculation.

A. The earlier study -- I'm not directly answering your question, perhaps, because it is speculation.

Q. I don't want you to speculate.

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A. -- did not use doses as high as what they used in this study. They also had a different patient population.

So it's possible that in this study they saw more adverse events because the patient population was different and the doses were higher.

So I would still believe that they're talking about 114 in this -- as the -- not justification, but they've seen what's going on in 114. They're holding this meeting.

Q. And that's based solely on the date of the document?

A. Dates of the document, yeah.

Q. And you're aware that the results in the M99-114 study were double-blinded until April of 2001; is that correct?

A. I can't swear to the date, but I know they were unblinded as of -- they were blinded up to the point that I was considering it.

Q. Okay. So up to the point of March 5th, 2001, which is the date of this document, you're aware the results were blinded?

A. Yes, I believe that's the case.

MR. ZWICKER: Is this a good time for

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him to amend another answer?

MS. GUZELSU: His second answer, yes.

A. The other document that I saw was a list of patients who were dropping out and the day on which they dropped out.

I can't put my finger on the document itself, but I remember the table showed what days people were dropping out and I believe the cause.

Now, the disturbing part about that table was that people were dropping out so early in the study. And that would have been disturbing to the people looking at the thing, too, because they were for adverse events.

Now, we had talked about the -- how many of the patients were providing -- of the dropouts were providing usable data. And now that I think about it, a lot of those were occurring early on, many of them in the titration phase of the study.

So there wouldn't be much data that you could get from those patients on the primary response variable. You'd have their baseline, perhaps. I think they were supposed to go through the titration phase before they started giving data on the primary variable.

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So my figures I think are not all that far off in terms of the power because I don't think you're going to be able to bring back much data from these dropout patients.

Q. Let's say you only had one -- you had the baseline piece of data, which is before they've been dosed, and then you have one piece of data after that, and that individual drops out for adverse events. Is it your opinion that that individual's data would not be used in the final analysis of the study?

MR. ZWICKER: Objection. Incomplete hypothetical.

A. You had one piece of primary response variable data?

Q. Yeah.

A. That person's data could be used in the study, but it doesn't weigh as much as somebody who completes the study.

Q. But you still have to use that person's data? You couldn't just disregard it?

A. In fact, you have to use it in the intent to treat analysis. It's how you use it that's the question.